COMBINATION UPDATE

FDA's New Draft Guidance on Technical Considerations for Pen, Jet & Related Injectors Intended for Use With Drugs & Biological Products: Comments & Concerns

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On April 27, 2009, the US FDA issued a new draft guidance document that was much-anticipated by many in the drug delivery world.[1] The draft guidance, *Technical Considerations for Pen, Jet, and Related Injectors Intended for Use with Drugs and Biological Products*, covers a wide array of injector products and topics.[2] It is of particular significance to companies that develop and manufacture therapeutic products administered by pen, jet and other types of injectors, as well as to medical device manufacturers that develop and make injectors. The FDA required comments to be submitted by July 27, 2009, to ensure they are reviewed before the agency started finalizing the guidance.[3]

The following provides an overview of the draft guidance and highlights some of the key comments submitted in response. Overall, stakeholders expressed several fundamental concerns regarding the guidance that, if adopted by the agency, will require major revisions. It remains to be seen how the agency will respond.

OVERVIEW OF THE DRAFT GUIDANCE

Scope

The draft guidance casts a wide net to a broad range of products in two important respects. First is the way in which injector is defined. It includes - but is not limited to - jet injectors, pen injectors, piston syringes, needle-free injectors, mechanically operated injectors, and injectors with computerized or electronic elements. Thus, the draft guidance encompasses several types of technologically diverse injectors and could include even more now or in the future. On the other hand, the guidance excludes some injectors, such as dental surgery jet injectors, without explaining why. Stakeholders commenting on the draft guidance expressed concern over how they could assess what other injectors may be included or excluded from the guidance's scope, given the lack of explanation on the definition.

Second, the draft guidance addresses nearly all configurations of injectors: stand-alone, general use injectors, injectors intended for a product class or product line, and injectors intended for use with a specifically named drug or biological product. In other words, the draft guidance extends to combination products of which a device injector is a constituent part, and to general use device injectors that are not combination products.[4] Here, commentors expressed confusion on what injectors are intended for a product class or product line and asked for examples of what the agency means.

Technical & Scientific Issues for Injectors

The draft guidance primarily focuses on the technical and scientific issues to be considered when developing injectors intended for use with drugs or biological products, as well as content and format information for injectors that are reviewed under a 510(k) submission or as part of an NDA or Biologics License Application (BLA). However, a significant concern expressed in comments is that, despite its wide breadth of scope, the draft guidance does little to differentiate among the requirements that may apply to different types of injectors. Instead, the document provides wide-ranging lists of scientific and technical considerations that may or may not be relevant depending upon the type of injector at issue. Though the information provided is quite comprehensive, the draft guidance fails to connect the information to specific types of injectors. This issue fundamentally impacts the structure and content of the guidance.

In addition to this key issue, commentors questioned the document's apparent inconsistency with other guidance documents, such as the FDA's *Guidance on the Content of Premarket Notification (510(k)) Submissions for Piston Syringes*, FDA device design control guidance, and the draft ISO document *Needle-Based Injection Systems for Medical Use - Automated Functions - Requirements and Test Methods*.

As a result, if the final version remains substantially as written, it could significantly increase regulatory burdens for injector marketing submissions, particularly the relatively simpler, general use device injectors. Applicants submitting injector-related marketing submissions would need to study the draft guidance carefully to glean the most pertinent information for their products.

Policy Considerations

Commentors also expressed a variety of concerns with the guidance's lack of discussion on policy issues impacting the development and approval of injectors. One example is with

respect to clinical studies on injector-related products, which the guidance addresses in a way that raises more questions than it answers. For example, while the draft guidance notes that specific considerations for clinical trial design are beyond its scope, it makes the broad statement that clinical trials for some injectors may focus on the injector itself without providing examples of this seemingly atypical situation. The current draft also does not acknowledge situations in which clinical trials may not be required or where simulated use studies may be preferred.

Further, although the draft guidance is directly focused on injector development and submissions, it fails to address a number of fundamental, intertwined policy issues. By way of example, the draft guidance does not provide much detail on the appropriate type(s) of marketing application for injector combination products. Thus, while the draft guidance provides detailed information on the content requirements of an application for an injector or incorporating an injector, it does not address fundamental questions about the type or number of application(s) required. Another example is the rules pertaining to device modifications, including any needed FDA submissions. As commentors observed, because general guidance on this issue for combination products is limited, manufacturers of combination products incorporating injectors have struggled with these ambiguities.

In addition to the aforementioned issues, commentors identified numerous concerns and questions with specific language and provisions in the draft guidance. Those interested in reviewing the submitted comments can obtain them on www.regulations.gov.[5]

SUMMARY

In all, the draft guidance could have important implications for both stand-alone injector products and injectors that are part of a drug-device or biological-device combination products, including potential significant increases in submission requirements. Manufacturers of injectors or products incorporating an injector component will want to review the draft guidance and track future FDA communications regarding plans to revise and finalize the guidance. ◆

REFERENCES

1. 74 Fed Reg. 19094, Draft Guidance for Industry and Food and Drug Administration Staff: Technical Considerations for Pen, Jet, and Related Injectors Intended for Use With Drugs and Biological Products. Availability April 27, 2009.
2. The draft guidance is available at: http://www.fda.gov/downloads/RegulatoryInformation/Guidances/UCM147095.pdf.
3. FDA regulations allow for public comment on guidance documents at any time.
4. This could be a drug-device or a biological-device combination that is combined or produced as a single entity or that is packaged or labeled for use in combination. See 21 CFR § 3.2(e).
5. Comments submitted on the draft guidance are available at: http://www.regulations.gov/search/Regs/home.html#docketDetail?R=FDA-2009-D-0179 (FDA Docket No. 2009-D-0179).

BIOGRAPHIES

Bradley Merrill Thompson is a shareholder in the Health Practice in Epstein Becker & Green's Washington, DC, office. Mr. Thompson counsels medical device, drug, and combination product companies on a wide range of issues involving compliance with the laws administered by the FDA, as well as reimbursement issues. He serves as General Counsel to the Combination Product Coalition and Counsel to AdvaMed for payment issues. In addition to a law degree, Mr. Thompson earned an MBA and often works with clients on strategic planning.

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